INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/35088

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07H 21/04; A61K 48/00
US CL : 536/24.5; 514/44
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 536/24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,998,588 A (HOFFMAN et al) 07 December 1999 (07.12.1999), see entire document.	1 and 22 --- 2-103
Y	ASTRIAB-FISHER et al. Conjugates of Antisense Oligonucleotides with the TAT and Antennapedia Cell-Penetrating Peptides: Effects on Cellular Uptake, Binding to Target Sequences, and Biologic Actions. Pharmaceutical Reasearch. June 2002, Vol. 19, No. 6, pages 744-754, see entire document.	1,22,29,36,37,38,57, 64,70,85,92,99,100-106
X, P	US 2003/0190635 A1 (MCSWIGGEN et al) 09 October 2003 (09.10.2003), see entire document.	1-109
Y	VERONESE et al. Bioconjugation in pharmaceutical chemistry. IL FARMACO. June 1999, Vol. 54, pages 497-516, see entire document.	1-103
Y	US 2002/0102267 A1 (LU et al) 01 August 2002 (01.08.2002), see especially page 20.	1-27, 34-62, 69-90, 97-109

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
04 February 2005 (04.02.2005)

Date of mailing of the international search report
24 MAR 2005

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2002/0151512 A1 (PEYMAN et al) 17 October 2002 (17.10.2002), see page 3.	1,3,7,8,10-28,36,37,101 --- 2,4-6,9,29-35, 38-100, 102, 103
Y	US 2002/0156235 A1 (MANOHARAN et al) 24 October 2002 (24.10.2002), see page 2.	1,22,29
A	FIRE, A. RNA-triggered gene silencing. TIG. September 1999, Vol. 15, No. 9, pages 358-363.	1-9, 38-45,70-76
A	MANOHARAN, M. Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery, and Mechanism of Action. Antisense & Nucleic Acid Drug Development. 2002, Vol. 12, pages 103-128.	1-109

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

I. Claims 1-37, drawn to a composition comprising a first and a second oligomeric compound, wherein atleast a portion of said first oligomeric compound is capable of hybridizing to a portion of the second, wherein atleast a portion of the first oligomeric compound is capable of hybridizing to a target nucleic acid, and wherein atleast one of the oligomeric compounds comprises atleast one conjugate moiety.

II. Claims 38-69, drawn to a composition comprising a first oligomeric compound capable of hybridizing to a target nucleic acid, optionally a second oligomeric compound hybridizable to said first oligomeric compound, atleast one protein (comprising a portion of RISC), wherein said composition comprises atleast one oligomeric compound comprising atleast on conjugate moiety.

III. Claims 70-100, drawn to an oligomeric compound comprising a first and a second region, wherein said first region is capable of hybridizing with said second region, wherein a portion of the oligomeric compound is capable of hybridizing to a target nucleic acid, and wherein said oligomeric compound further comprises atleast one conjugate moiety.

IV. Claims 101-103, drawn to pharmaceutical compositions comprising one of the compositions of the first three groups.

V. Claims 104-109, drawn to methods of modulating the expression of the target nucleic acid and methods of treating or preventing a disease or disorder.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of claim 1 is drawn to a composition comprising a first and second oligomeric compound, wherein atleast a portion of said first compound is capable of hybridizing to a portion of said second compound, wherein atleast a portion of said first oligomeric compound is capable of hybridizing to a target nucleic acid, and wherein atleast one of said first and said second oligomeric compounds comprises atleast one conjugate moiety. Claim 1 broadly reads on all oligonucleotides with conjugate moieties. Wickstrom et al. (US6180767, abstract) teach peptide nucleic acid (PNA) oligomers that are conjugated to a ligand in order to facilitate cellular uptake of the PNA oligomer. Further, the PNA oligomer base sequence is selected to hybridize to a target polynucleotide sequence by either triplex (dsDNA) or duplex (ssDNA;RNA) formation. This meets the structural limitations of claim 1 and is considered to have the functionality recited therein. Therefore, there is no special technical feature.